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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/904,356	07/12/2001	Graham P. Allaway	43966-CB/JPW/SHS	2885

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EXAMINER	
PARKIN, JEFFREY S	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 11/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/904,356	ALLAWAY ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-9 and 13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-9 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Response to Amendment

Status of the Claims

Acknowledgement is hereby made of receipt and entry of the amendment filed 20 February, 2004, wherein claims 1-6 and 10-12 were canceled without prejudice or disclaimer, claims 7 and 8 amended, and new claim 13 introduced. Claims 7-9 and 13 are pending in the instant application.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

Claims 7-9 and 13 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *In re Rasmussen*, 650 F.2d 1212, 211 U.S.P.Q. 323 (C.C.P.A. 1981). *In re Wertheim*, 541 F.2d 257, 191 U.S.P.Q. 90 (C.C.P.A. 1976). The claims are directed toward methods of inhibiting macrophage-tropic HIV-1 fusion to a $CD4^+$ cell target through the administration of an "agent" that inhibits HIV-1 macrophage-tropic fusion events without inhibiting HIV-1 T-cell tropic fusion events. The disclosure describes a fluorescent resonance energy transfer (FRET) assay that is useful for studying membrane fusion events mediated by the HIV-1 envelope. Preliminary evidence suggests that certain β-chemokines

(e.g., MIP-1α) may inhibit primary, NSI, Env fusion interactions without affecting SI fusion events. However, this interaction appeared to be cell-depedent. Another inhibitory molecule (e.g., OKT4A) was non-specific and inhibited both NSI- and SI-Env mediated events. The claims encompass a large genus of poorly defined chemical compounds which could include, inter alia, antibodies, organic compounds, small molecular weight polypeptides, peptidomimetics, and retroinverso peptides.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Vas-Cath, Inc., v. Mahurkar*, 935 F.2d at 1563, 19 U.S.P.Q.2d at 1116. The issue raised in this application is whether the original application provides adequate support for the broadly claimed genus of "agents" that display preferential inhibitory activities toward NSI-Env mediated events but not SI-Env mediated events. As set forth supra, this genus has not structural boundaries and could encompass, inter alia, antibodies, organic compounds, small molecular weight polypeptides, peptidomimetics, and retroinverso peptides.

An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997). The claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by functional characteristic,

without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the biomolecule of interest. *In re Bell*, 991 F.2d 781, 26 U.S.P.Q.2d 1529 (Fed. Cir. 1993). *In re Deuel*, 51 F.3d 1552, 34 U.S.P.Q.2d 1210 (Fed. Cir. 1995). A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 U.S.P.Q.2d 1895, 1905 (Fed. Cir. 1995). The court noted in this decision that a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not reasonably lead those skilled in the art to any particular species.

An applicant may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole. An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. For some biomolecules, examples of identifying characteristics include a nucleotide or amino acid sequence, chemical structure, binding affinity, binding specificity, and molecular weight. The written description requirement may be satisfied through disclosure of function and minimal structure when there is a well-established correlation between structure and function. Without such a correlation, the

capability to recognize or understand the structure form the mere recitation of function and minimal structure is highly unlikely. In the latter case, disclosure of function alone is little more than a wish for possession; it does not satisfy the written description requirement. *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1566, 43 U.S.P.Q.2d 1398, 1404, 1406 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089 (1998). *In re Wilder*, 736 F.2d 1516, 1521, 222 U.S.P.Q. 369, 372-3 (Fed. Cir. 1984). Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention.

The disclosure fails to provide any guidance pertaining to the molecular determinants modulating NSI/SI-Env mediated events. Rationale drug design is facilitated by a knowledge of those regions that are critical for envelope interactions. In the absence of such information, the skilled artisan is essentially being asked to guess as to which agents or compounds might function in the desired manner. The disclosure also fails to provide any guidance pertaining to the structure of any given "agent". The specification provides a small number of β-chemokines that may inhibit NSI-Env-mediated events in a cell-dependent matter. However, no other agents or molecules meeting the requirements are disclosed. Finally, the lack of a structural/functional correlation fails to lead the skilled artisan to any particular compound. Accordingly, the skilled artisan would reasonbly conclude that applicants were not in possession of the claimed invention at the time of filing.

Applicants traverse and submit that the disclosure provides sufficient written support for the claimed invention. This argument is not persuasive for the reasons set forth *supra*. Moreover,

applicants' response fails to provide any objective scientific data addressing the aforementioned caveats. Moreover, the molecular determinants modulating HIV-1 envelope fusion are complex (O'Brien *et al.*, 1990). The description provides a generic screening assay for identifying putative macrophage-tropic-specific or T-cell-tropic-specific inhibitors. However, this screening assay fails to provide any guidance pertaining to the structure of those compounds that can reasonably be expected to inhibit viral cell fusion. The skilled artisan cannot reasonably predict the structure of any given inhibitor. Furthermore, the disclosure fails to provide sufficient guidance pertaining to this point. While the disclosure describes the isolation of four Mabs (PA-3, PA-5, PA-6, and PA-7) that are capable of inhibiting envelope-mediated viral cell fusion, none of these compounds were specific to either macrophage-tropic or T-cell-tropic isolates. The disclosure clearly stated (p. 60, first paragraph) that "The culture supernatants from hybridomas PA-3, PA-5, PA-6 and PA-7 inhibited fusion between HeLa-env_{JR-FL} and PM1 cells in the RET assay, and also inhibited fusion between HeLa-env_{LAI} cells and certain CD4+ target cells (Table 3)." Thus, the disclosure fails to identify any suitable agents with the desired properties. Thus, upon perusal of the disclosure, the skilled artisan would reasonably conclude that applicants were not in possession of a reasonable number of macrophage-tropic- or T-cell-tropic-specific inhibitory agents. Finally, nothing in the disclosure points the skilled artisan toward any particular class of agents. Accordingly the rejection is proper and hereby maintained.

Scope of Enablement

Claims 7-9 and 13 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not reasonably enable any person skilled in the art to which it pertains, or with which it is

most nearly connected, to make and/or use the invention commensurate in scope with these claims. The claimed invention is directed toward methods of inhibiting macrophage-tropic HIV-1 fusion to a $CD4^+$ cell target through the administration of an agent or compound that is specific only for macrophage-tropic isolates or methods of inhibiting T-cell tropic HIV-1 fusion to a $CD4^+$ cell target through the administration of an agent or compound that is specific only for T-cell tropic isolates.

The legal considerations that govern enablement determinations pertaining to undue experimentation are disclosed in *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988) and *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows: **1) The disclosure fails to provide adequate guidance pertaining to the molecular determinants that are specific to macrophage-tropic envelope-mediated cell fusion and T-cell-tropic envelope-mediated cell fusion.** Rationale drug development requires a knowledge of the molecular determinants that are specific to each type of virus. This would provide a starting point for the skilled artisan to begin testing compounds in the hope of identifying something useful. However, the disclosure fails to provide any guidance pertaining to this consideration. Moreover, the disclosure fails to provide a reproducible method for identifying putative inhibitors. While a fusion assay is provided in the specification, the skilled

artisan cannot reasonably predict which compounds or agents will function in the desired manner.

2) The disclosure fails to provide adequate guidance pertaining to the structural requirements of any given inhibitor. The disclosure fails to describe any particular class of compounds that can reasonably be expected to function in the desired manner. Absent any guidance concerning the structure of said compounds, an undue invitation to further experimentation has been extended to the skilled artisan.

3) The claims are of considerable breadth and encompass an inordinate number of compounds. However, as noted *supra*, the disclosure fails to provide sufficient guidance pertaining to the molecular determinants modulating macrophage-tropic-specific and T-cell-tropic-specific fusion interactions. The disclosure also fails to provide any guidance pertaining to the structure of any given inhibitory agent. Thus, the specification clearly fails to support the breadth of the claimed invention.

4) The disclosure fails to provide a sufficient number of working embodiments. Considering the breadth of the claimed invention, a representative number of working embodiments would be required. However, the specification is deficient in this regard. Moreover, the disclosure clearly illustrates the problems associated with identifying specific inhibitors wherein it was reported (p. 60, first paragraph) that "The culture supernatants from hybridomas PA-3, PA-5, PA-6 and PA-7 inhibited fusion between HeLa-env_{JR-FL} and PM1 cells in the RET assay, and also inhibited fusion between HeLa-env_{LAI} cells and certain CD4+ target cells (Table 3)." Therefore, when all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation from the skilled artisan to practice the claimed invention.

Applicants traverse and submit that the specification fully supports the breadth of the claimed invention. This argument is not

tenable for the reasons set forth *supra*. Applicants' response fails to provide any objective scientific data that addresses the various caveats set forth. Accordingly the rejection is proper and hereby maintained.

Finality of Office Action

Applicants' amendment necessitated any and all new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). **A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.**

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, James C. Housel, can be reached at (571) 272-0902. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Formal communications may be submitted through the official facsimile number which is (703) 872-9306. Hand-carried formal communications should be directed toward the customer window located in Crystal Plaza Two, 2011 South Clark Place, Arlington, VA. Applicants are directed toward the O.G. Notice for further guidance. 1280 O.G. 681. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-

0908.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

Jeffrey S. Parkin, Ph.D.
Primary Examiner
Art Unit 1648

12 November, 2004